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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,138	11/06/2006	David Wallach	30694/41889	3144

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EXAMINER	
WEN, SHARON X	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/573,138	WALLACH ET AL.	
	Examiner	Art Unit	
	SHARON WEN	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 19-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 19-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment, filed 06/02/2010, has been entered.

Claims 18, 57-64 and 84-85 have been canceled.

Claims 1-17, 19-56 and 65-83 are pending.

Claims 17, 39-56 and 65-83 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention/species, there being no allowable generic or linking claim.

Claims 1-16 and 19-38 are currently under examination as they read on a composition or a preparation comprising an antibody that binds a peptide of NIK set forth in SEQ ID NO: 7, 11 or 12, the hybridoma producing the antibody.

This Action will be in response to Applicant's Arguments/Remarks, filed 06/02/2010.

The rejections of record can be found in the previous Office Action, mailed 12/03/2009.

New Grounds of rejection necessitated this Office Action being Non-Final.

Claim Objections

The previous claim objection has been withdrawn in view of Applicant's amendment, filed 06/02/2010.

Claim Rejections - 35 USC § 112 second paragraph

The previous claim rejection under 35 USC 112 second paragraph has been withdrawn in view of Applicant's amendment, filed 06/02/2010.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The previous scope of enablement rejection for the recitation of "a CDR" in claims 8 and 37 been withdrawn in view of Applicant's amendment, filed 06/02/2010. Furthermore, Applicant's assurance that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications in the remarks, filed 06/02/2010, has obviated the previous rejection for a biological deposit.

Claims 1-16 and 19-38 **stand** rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody that binds the amino acid sequence set forth in SEQ ID NO: 7, 11 or 12, does not reasonably provide enablement for an antibody that binds **any** portion of the amino acid sequences set forth in SEQ ID NO: 7, 11 or 12 for detecting NIK **or a mutein, functional derivative, active fraction, circularly permutated derivative, salt or a portion thereof**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Applicant's argument has been considered but has not been found convincing for reasons of record and reiterated herein for Applicant's convenience.

> Under the broadest reasonable interpretation, the present claims are broadly drawn to antibodies that bind to an amino acid sequence or a portion of the amino acid sequence which reads on variants or fragments of the peptides with any minimal consecutive 2 amino acids. However, other than the antibodies binding to the amino acid sequence set forth in SEQ ID NOs: 7, 11 or 12, there does not appear to be an actual reduction to practice of an antibody that binds other species of the genus encompassing the variants of SEQ ID NOs: 7, 11 or 12; nor is there a complete or partial structure of an antibody capable of binding all the species of the above mentioned genus in detailed drawing or through a structural chemical formula, e.g., sequence of the antibody.
>
> Furthermore, a skilled artisan is well aware that such antibodies binding the amino acid sequences of SEQ ID NOs: 7, 11 or 12 would not reasonably be expected to be reactive with all members of the genus encompassing all the variants of the peptides. For example, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991; see entire document) disclosed that a single amino acid

substitution in a common allele ablates binding of a monoclonal antibody. Further, Li et al. (PNAS 77: 3211-3214, 1980; see entire document) disclosed that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document). Moreover, for instance, Houghten et al. (New Approaches to Immunization, Vaccines 86, Cold Spring Harbor Laboratory, p. 21-25, 1986) taught the criticality of individual amino acid residues and their positions in peptide antigen-antibody interactions. Houghten et al. state (see page 24): "One could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance of the binding interaction of the altered residue. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool."

Give that the instant specification disclosed that the claimed antibody is used for detection of NIK or a mutein, functional derivative, active fraction, circularly permutated derivative, salt or a portion thereof. One of skill in the art would not be able to use the antibody that binds to SEQ ID NO: 7, 11 or 12 to measure all the variants of SEQ ID NO: 7, 11 or 12 or detect NIK or a mutein, functional derivative, active fraction, circularly permutated derivative, salt or a portion thereof, because, as the state of the art discussed above, the antibody that binds SEQ ID NO: 7, 11 or 12 would not be able to bind to all the variants of the peptides or NIK.

Therefore, the specification, as-filed, provided insufficient guidance to lead a person of skill in the art to use the claimed antibodies that binds SEQ ID NO: 7, 11 or 12 to measure all the variants of SEQ ID NO: 7, 11 or 12 commensurate in scope of the instant disclosure.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

In response to Applicant's argument that one of ordinary skill in the art would have the requisite skill to generate anti-NIK antibodies having in hand the NIK peptides encoded by the amino acid sequences recited in the claims using the specification as a guide, it is noted that the issue there is that one of skill in the art would not be able to use an antibody that binds *any portion* of the recited sequences to detect NIK because an antibody that binds any portion of the recited sequence would not necessarily have the specificity for NIK. The binding of antibody to antigen is highly specific as discussed in the previous Office Action (see above for Lederman et al., Li et al., and Houghten et

al.). The present claims recite "*a portion of said amino acid sequence*" and require the antibody to be capable of detecting NIK in a Western blot, ELISA or immunoprecipitation assay. "*A portion* of the amino acid sequence" reads on any fragment of the amino acid sequence and encompasses as few as one amino acid. Given the unpredictability in the art pertaining to changing sequence in the antigen and retaining antibody binding capability as taught by Lederman et al., Li et al., and Houghten et al., and in view of lack of teaching by the instant specification on making or using an antibody that binds to sequences other than the full length SEQ ID NO: 7, 11 or 12, one of skill in the art would not be able to make or use antibodies that binds to as few as one amino acid of SEQ ID NO: 7, 11 or 12 and retain its binding capacity to NIK in order to detect NIK in Western, ELISA or immunoprecipitation assay without undue experimentation. Similarly, antibodies that bind specifically to SEQ ID NO: 7, 11 or 12 would not be able to bind all the muteins, functional derivative, active fraction, circularly permutated derivative or salt of NIK because these variants of NIK represent a genus encompassing different amino acid sequences.

Applicant's argument has not been found convincing. Therefore, this rejection is maintained as it applies to amended claims.

Applicant is invited to amend the claims to recite "the amino acid sequence of SEQ ID NO: 7, 11 or 12" and avoid the recitation of "a portion thereof" and "a mutein, functional derivative, active fraction, circularly permutated derivative, salt or a portion thereof" in order to obviate this rejection.

New Grounds of rejection are set forth below:

Claims 1-16 and 19-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Regarding the instant claim limitations, the specification does not appear to provide an adequate written description for the all various portions of SEQ ID NO: 7, 11 or 12, and all muteins, functional derivatives, active fractions, circularly permutated derivatives, salts of NIK as targets of the claimed antibodies because there is a lack of sufficient written description to support the recited genus of the antibody targets.

The standard for Written Description is met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." See Enzo Biochem., Inc. v. Gen-Probe Incorporated 323 F.3d 956 (Fed. Cir. 2002).

The instant specification disclosed that the polypeptide set forth in SEQ ID NO: 7, 11 and 12 are epitopes to which anti-NIK antibodies. However, the present claims are drawn to a genus of the antibody targets that encompasses any portions of SEQ ID NO: 7, 11 or 12 and various muteins, functional derivatives, active fractions, circularly permutated derivatives, salts of NIK.

The fact that two polypeptides that are homologous in structure or share certain degrees of identity in sequence does not in and of itself required that the two sequences share any functional activity such as anti-microbial activity. In the absence of sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, the claimed invention is not described in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of all various portions of SEQ ID NO: 7, 11 or 12, and all muteins, functional derivatives, active fractions, circularly permutated derivatives, salts of NIK as targets of the claimed antibodies.

A person of skill is well aware, at the time of the invention was made, that different molecules, even with sequence similarity, do not necessarily have the same function. For example, Attwood (Science 290: 471-473, 2000) teaches that “[i]t is presumptuous to make functional assignments merely on the basis of some degree of

similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 18: 34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

Therefore, the disclosed amino acid sequences set forth in SEQ ID NOs: 7, 11 and 12 are not sufficiently representative of the genus encompassing all portions of SEQ ID NO: 7, 11 or 12 and the sequence of NIK is not sufficiently representative of all muteins, functional derivatives, active fractions, circularly permutated derivatives, salts of NIK as targets of the claimed antibodies because the disclosure fails to describe the common attributes or characteristics that identify all members of the genus, known and unknown at the time the invention was made.

As the fragments and variants of NIK are the targets of the recited antibody, Applicant has not provided a sufficient written description of all the antibodies that are capable of binding to all the targets for the following reasons.

Other than the antibody binding to the SEQ ID NO: 7, 11 or 12, there does not appear to be an actual reduction to practice of an antibody that binds other species of the genus encompassing all fragments of SEQ ID NOs: 7, 11 and 12 and all the muteins, functional derivatives, active fractions, circularly permutated derivatives, salts of NIK; nor is there a complete or partial structure of an antibody capable of binding all the species of the above mentioned genus in detailed drawing or through a structural chemical formula, e.g., sequence of the antibody.

Furthermore, a skilled artisan is well aware that such antibodies binding SEQ ID NO: 7, 11 or 12 would not reasonably be expected to be reactive with all members of the genus encompassing all fragments of SEQ ID NOs: 7, 11 and 12 and all the muteins, functional derivatives, active fractions, circularly permutated derivatives, salts of NIK.

For example, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991; see entire document) disclosed that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody. Further, Li et al. (PNAS 77: 3211-3214, 1980; see entire document) disclosed that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document). Moreover, for instance, Houghten et al. (New Approaches to Immunization, Vaccines 86, Cold Spring Harbor Laboratory, p. 21-25, 1986) taught the criticality of individual amino acid residues and their positions in peptide antigen-antibody interactions. Houghten et al. state (see page 24): "One could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance of the binding interaction of the altered residue. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool."

Therefore, the specification does not provide for sufficient written description to reasonably convey to one skilled in the relevant art that, at the time the application was filed, Applicant had possession of all antibodies capable of binding to all the fragments of SEQ ID NOs: 7, 11 and 12 and all the muteins, functional derivatives, active fractions, circularly permutated derivatives, salts of NIK.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See Vas-Cath at page 1116.) Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision. (See page 1115.)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-16 and 30-38 stand rejected under 35 U.S.C. 102(e) as being anticipated by Schreiber et al. (US 6,822,138 B1, see entire document).

Applicant's argument has been considered but has not been found convincing for reasons of record and reiterated herein for Applicant's convenience.

> Schreiber taught a polyclonal antibody that binds specifically to NIK (see e.g., column 15, paragraph 4) and a pharmaceutical composition comprising the antibody as a modulator of NIK and a pharmaceutically acceptable carrier (see column 18, lines 41-49 and column 27, lines 32-43).
>
> Although Schreiber et al. did not teach the polyclonal antibody to NIK to bind specifically to the peptides set forth in SEQ ID NO: 7, 11 or 12, given that polyclonal antibodies are known to bind multiple epitopes on one antigen, the prior art polyclonal antibody raised against NIK would necessarily bind to the epitopes comprising the amino acid sequences of SEQ ID NO: 7, 11 and 12.
>
> Since the Office does not have a laboratory to test the prior art polyclonal antibody, it is Applicant's burden to provide objective evidence showing that Schreiber's polyclonal antibody raised against NIK does not bind to SEQ ID NO: 7, 11 or 12.

In response to Applicant's argument that Schreiber disclosed a genus of antibodies that bind NIK and does not each the specific antibody that binds the recited sequences in the instant claims, it is noted that the polyclonal antibody taught by Schreiber would more likely than not bind SEQ ID NO: 7, 11 and 12 because polyclonal antibodies are known in the art to bind multiple epitopes. The burden was properly shifted to Applicant to provide objective evidence to show that Schreiber's polyclonal antibody does not bind SEQ ID NOs: 7, 11 and 12. Applicant's amendment has not

been found convincing. Therefore, the rejection is maintained for reasons of record as it applies to the amended claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON WEN whose telephone number is (571)270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571)272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sharon Wen/
Examiner, Art Unit 1644
August 15, 2010